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Effects of Drinking Water Monochloramine on Lipid and Thyroid Metabolism in Healthy Men

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The purpose of this study was to determine whether a 4-week consumption of 1.5 L per day of drinking water containing monochloramine at a concentration of 2 ppm (ppm = mg/L) or 15 ppm under controlled conditions would alter parameters of lipid or thyroid metabolism in healthy men. Forty-eight men completed an 8-week protocol during which diet (600 mg cholesterol per day, 40% calories as fat) and other factors known to affect lipid metabolism were controlled. During the first 4 weeks of the protocol, all subjects consumed distilled water. During the second 4 weeks, one-third of the subjects were assigned randomly to drink 1.5 L per day of water containing 2 ppm of monochloramine, to drink 1.5 L per day of water containing 15 ppm monochloramine, or to continue drinking distilled water. Four blood samples were collected from each subject at the end of each 4-week study period. Subjects drinking monochloramine at a concentration of 2 ppm showed no significant changes in total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, apolipoproteins A1, A2, or B when compared to the distilled water group. Parameters of thyroid function also were unchanged by exposure to monochloramine at this concentration. However, subjects drinking monochloramine at a concentration of 15 ppm experienced an increase in the level of apolipoprotein B. Other parameters of lipid and thyroid metabolism did not change. We conclude that consumption of drinking water containing 2 ppm of monochloramine does not alter parameters of lipid and thyroid metabolism in healthy men. Consumption of water containing 15 ppm monochloramine may be associated with increased levels of plasma apolipoprotein B.

Introduction

Exposure of humans to chlorinated drinking water disinfectants is almost universal in the United States (*1*). Chlorine is the disinfectant used by the majority of public water systems that disinfect their water, but chloramine is also used in a number of areas at present. Moreover, it has been suggested that chloramine would be the preferred agent to use with newer disinfectants such as ozone in order to achieve an effective residual of disinfectant in water distribution systems.

Revis and colleagues have studied the effect of drinking water chlorine and monochloramine on lipid and thyroid metabolism in white Carneau pigeons (*2*). Pigeons consuming a high-fat, high-cholesterol, low-calcium diet experienced a significant increase in serum cholesterol and a decrease in serum thyroxine when given chlorinated water to drink. Similar findings were seen with monochloramine at 2 ppm (ppm = mg/L) and 15 ppm. These effects were observed at concentrations of drinking water disinfectants near the range typically consumed by humans.

Investigations of the effects of chlorine and monochloramine on human lipid and thyroid metabolism are limited. Lubbers and colleagues exposed healthy human volunteers to low and high concentrations of chlorine, monochloramine, and other chlorinated disinfectants for brief intervals and observed no effect on total cholesterol levels (*3*). More prolonged exposure to 5 ppm chlorine and monochloramine also had no apparent effect. However, diet and the intake of other liquids possibly containing chlorinated disinfectants were uncontrolled, so these studies do not effectively exclude the possibility that chlorine or monochloramine affects human lipid metabolism.

Wones and colleagues have conducted two studies of drinking water chlorine and human lipid metabolism. The first was an uncontrolled 15-week dose–response trial of drinking water chlorine (0, 2, 5, 10 ppm) in 19 healthy men in which a clinically small increase (3%) in total cholesterol levels at chlorine concentrations of 5 ppm and 10 ppm was observed (*4*). However, no control group was studied, and it is possible that the observed increase was due to the protocol diet or other factors and not to the chlorine.

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The second study was a controlled 8-week study involving 30 men and 30 women (5). All subjects drank distilled water for the first 4 weeks of the protocol. Half were randomized to receive chlorinated drinking water (20 ppm) for the next 4 weeks, while the other half continued to drink distilled water. No effect on parameters of lipid or thyroid metabolism was observed from this short-term exposure to chlorine.

Zeighami and colleagues have reported an epidemiological study of 40 small Wisconsin communities, 20 of which chlorinated their water supply and 20 of which did not chlorinate their water supply (6). Older women (40–60 years) living in communities with chlorinated supplies appeared to have slightly higher total cholesterol levels (about 5%) than women living in communities with unchlorinated supplies, though there was no significant difference found for men. No similar epidemiological data are available for monochloramine.

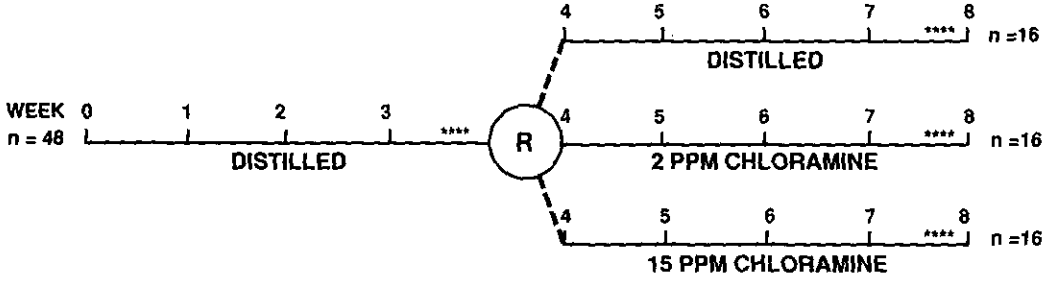
Thus, studies in humans are insufficient either to confirm or to exclude an effect of monochloramine in drinking water on human lipid or thyroid metabolism. The purpose of this study was to determine if drinking water containing monochloramine at concentrations of 2 ppm or 15 ppm would affect parameters of lipid or thyroid metabolism in healthy men unselected for baseline total cholesterol levels.

Methods

This study was a randomized, controlled, parallel trial of 8 weeks' duration. Neither the subjects nor the investigators were blinded as to who received monochloramine and who did not. The study protocol is illustrated in Figure 1. The protocol consisted of a 4-week dietary stabilization period during which all subjects drank distilled water buffered with sodium monophosphate to a pH of 8.5. The purposes of the baseline period were to achieve stabilization on a high-fat, high-cholesterol diet and to allow the effects of prior exposure to chlorinated water to dissipate. The baseline period was followed by a 4-week treatment period during which one-third of the subjects were assigned randomly to continue consuming buffered distilled water (distilled group), one-third were assigned to consume 1.5 L per day of drinking water containing 2 ppm monochloramine buffered with sodium monophosphate to a pH of 8.5 (2 ppm group), and one-third were assigned to consume 1.5 L per day of water containing 15 ppm monochloramine buffered to pH 8.5 (15 ppm group). The alkaline pH was used to mimic natural drinking waters, most of which are alkaline, and to ensure that the monochloramine did not become dichloramine. The trial was conducted in the General Clinical Research Center (GCRC) at the University of Cincinnati Hospital and was approved by its Institutional Review Board. All subjects gave written informed consent to participate.

Inclusion criteria for the study included healthy men between the ages of 18 and 65 years, no medications, and no concurrent illnesses. Screening total cholesterol measurements before enrollment into the study were performed for all potential subjects. Men who met the inclusion criteria were selected for study in such a way that one-fourth had screening total cholesterol measurements in each quartile for their age according to the Lipid Research Clinic's Prevalence Study (7). Subjects were stratified by screening total cholesterol quartile before randomization into groups so that each group included equal numbers of high-, middle-, and low-cholesterol subjects.

The study used one monochloramine concentration (2 ppm) in the range typically found in public water systems and one monochloramine concentration (15 ppm) somewhat higher than that usually found in public water systems. These concentrations were the same as those at which Revis found effects in pigeons (2). Drinking water for each subject was prepared by standard



DRINKING WATER: Distilled = 1.5 liter per day distilled water buffered to pH 8.5 with $NaHPO_4$
Chloramine = 1.5 liter per day distilled water with chloramine added and buffered to pH 8.5 with $NaHPO_4$

DIET: Isocaloric; 20% protein, 40% carbohydrate; 600 mg cholesterol per day; P:S ratio 0.4

LABORATORY: * Total Cholesterol, Triglycerides, HDL-C, LDL-C (calculated), T4, T3, T3 resin uptake, TSH, apolipoproteins A1, A2,and B.

R: Randomization

FIGURE 1. Study protocol.

procedures. Water was distilled and filtered through activated charcoal to remove any trace organic impurities. Before launching the study, samples of the resulting purified water were submitted to the Environmental Protection Agency (EPA) Health Effects Research Laboratory in Cincinnati and were judged to be free of trace organic impurities.

A sodium monophosphate buffer solution was prepared by dissolving 60 g NaH_2PO_4 in 500 mL distilled water and adjusting the pH to 8.5 with 2N NaOH. This solution was diluted to 1.0 L with distilled water. A concentrated monochloramine solution was prepared as follows: 1 mL of a concentrated ammonium hydroxide (28%) solution and 160 mL of the buffer solution described above were mixed in 3400 mL distilled water. Then, 13 mL of a concentrated chlorine solution (chlorine gas bubbled into a 1.0 L solution of 240 g/L NaOH until the pH falls to 12.0) were added to 500 mL distilled water. The pH of the chlorine solution and the pH of the buffered ammonium hydroxide solutions were adjusted as necessary to pH 8.5 with HCl. The chlorine solution was then added immediately to the ammonium hydroxide solution with constant stirring. The concentration of the final solution was 100–120 mg/L (as chlorine). Each day, GCRC dietary staff mixed an aliquot of the concentrated monochloramine solution with distilled water to prepare that day's drinking water for each subject. The final pH and chlorine concentration of one subject's drinking water was checked each day to assure that subjects actually received the appropriate concentration of monochloramine. Each subject's daily drinking water was prepared and stored in a well-marked thermos.

Subjects were also provided with a thermos of distilled water free of monochloramine and buffer, which they could drink at their option in addition to the 1.5 L of study water which they had to drink. Consumption of mandatory and optional water was monitored by daily checks of subjects' thermoses. Twenty-four-hour fluid intakes were recorded daily.

The study diet was designed individually to satisfy the food preferences of each subject and to be isocaloric. Each subject's diet plan was adjusted as necessary by a GCRC dietitian to maintain the subject at his or her admission weight. The diet consisted of 20% protein, 40% carbohydrate, and 40% fat. It contained 600 mg of cholesterol/day and a polyunsaturated to saturated fat ratio of 0.4. Dietary calcium was restricted to 80% of the minimum daily requirement for American adults.

The characteristics of the study diets were designed to mimic Revis' study in pigeons (*2*). Therefore the study diets were relatively high in total fat, saturated fat, and cholesterol. Despite the high fat and cholesterol content, such diets are not unusual for many Americans. Only over the last decade have Americans consumed less fat and cholesterol on average (*8*). The calcium restriction also reflects nutritional patterns in this country since many people, especially women and older Americans, consume a diet containing 80% or less of the recommended daily allowance of calcium (*9*). Study diets were formulated to avoid foods that contain chlorine (i.e., bleached flour). Thus, the study diets were designed to maximize the potential for observing a small effect of monochloramine on lipid and thyroid metabolism, minimize the influence of extraneous dietary confounders, and preserve generalizability.

All food was prepared in the GCRC kitchen. Two daily meal plans were used for each subject so that each person ate the same meals every other day for 56 days. Subjects were required to eat at least two meals and to drink the 1.5 L of study drinking water each day in the GCRC under observation. A third meal and a snack were packed for those subjects who wanted to consume them at home or at work. Subjects were instructed not to eat or drink anything that had not been provided for them.

Other lifestyle factors which might affect lipid or thyroid levels were controlled as well as possible. Subjects were not permitted to drink alcohol. If they smoked cigarettes, they were asked to keep their smoking constant throughout the study. They kept diaries of exercise activities and were also asked to keep their exercise habits constant. Subjects were required to refrain from swimming during the study to avoid exposure to chlorine from pool water.

Weight, blood pressure, pulse rate, and temperature were measured each morning in a fasted state by a GCRC staff nurse. Blood was drawn at entry to the study and weekly for total cholesterol, triglycerides, and HDL cholesterol (HDL-C). These tests were obtained daily for 4 consecutive days at the end of the baseline and treatment periods (week 4, week 8). Blood was drawn also on 4 consecutive days at the end of the baseline and treatment periods for apolipoproteins A1, A2 and B, thyroxine (T4), triiodothyronine (T3), T3 resin uptake, and thyroid-stimulating hormone (TSH). On days 0, 28, and 56, safety tests (serum electrolytes, blood urea nitrogen and creatinine, glucose, liver transaminases and alkaline phosphatase, calcium and phosphorous, urinalysis, white and red blood cell counts, reticulocyte count, and methemoglobin) were drawn. Glucose 6-phosphate dehydrogenase (G6PD) was measured upon entry into the study to detect individuals who might be susceptible to hemolytic anemia due to the oxidizing effects of monochloramine. None of the subjects was G6PD deficient.

All blood samples were drawn from the antecubital veins of supine subjects. Blood for lipid, lipoprotein, and apolipoprotein analyses were collected in sodium/potassium ethylenediaminotetracetate (EDTA, 1 mg/mL) anticoagulated tubes, and the plasma was rapidly separated by centrifugation and frozen at −20°C. All samples from individual subjects were analyzed as a batch at the end of the protocol. Total cholesterol, triglycerides, and HDL cholesterol were measured by microenzymatic procedures, standardized, and monitored through the Center for Disease Control's Lipid Standardization Program (*10*). HDL was isolated using the modified heparin-manganese chloride procedure (*11*). Interference in the enzymatic procedure was eliminated by the addition of 8 mEq/L of EDTA to the cholesterol reagent (*12*). Apolipoproteins (apo) A1 and B were quantitated by electroimmunoassay (*13*) and apo A2 by enzyme-linked immunoabsorbant assay (*14*). LDL cholesterol (LDL-C) was calculated as total cholesterol minus HDL-C minus triglycerides divided by 5. The other tests listed above were performed by the clinical laboratories of the University of Cincinnati Hospital using standard procedures.

Results of the lipid and thyroid function tests were analyzed as follows. For each subject, the mean of the four consecutive daily measurements during week 4 was considered the "baseline" value and the mean of the four daily measurements during week 8 the "treatment" value. The "change" value for each person was defined as the treatment value minus the baseline value. The means of the change values for the three groups were compared

using a one-way analysis of variance. Pairwise *t*-tests were used to compare each chloramine group with the distilled group if the ANOVA suggested that a significant difference of the means existed. A comparison of the weekly values of total cholesterol, triglycerides, and HDL-C was made also using a repeated measures analysis of variance. All *p*-values are two-tailed.

Results

Forty-eight men entered the study protocol and all completed it. Demographic data for the subjects by group are shown in Table 1. There were no statistically significant differences between the groups for age, weight, or entry total cholesterol.

Baseline, treatment, and change lipid and thyroid function test results for the subjects in the monochloramine and distilled water groups are shown in Table 2. The thyroid data for one subject in the 15 ppm monochloramine group were excluded before analysis because he was found to be chemically hypothyroid (low T4, high TSH) over the duration of the study. Inclusion of his thyroid results did not change the results of the analysis, but it would have made the baseline and treatment levels of T4 appear much lower and the mean level of TSH much higher than the other two groups.

There were no differences between the monochloramine and distilled water groups for changes in any of the parameters of

Table 1. Demographic data of male subjects.

	Group		
	Distilled water	Chloramine, 2 ppm	Chloramine, 15 ppm
Number of subjects	16	16	16
Age, years			
Mean ± SD	26.9 ± 7.2	27.8 ± 6.8	27.2 ± 6.0
Range	21–50	23–47	21–39
Weight, kg			
Mean ± SD	77.2 ± 10.7	72.5 ± 9.6	74.6 ± 6.4
Range	66–107	60–98	61–83
Total cholesterol at entry, mg/dL			
Mean ± SD	171.4 ± 29.6	172.6 ± 34.9	173.1 ± 30.4
Range	105–234	107–262	137–244
Race			
Caucasian	14	14	15
Black	1	2	1
Other	1	0	0
Previous source of drinking water			
Tap	13	14	13
Bottled	3	2	3
Well	0	0	0

Table 2. Effects of monochloramine on lipid and thyroid metabolism in men.[a]

Parameter	No. of subjects	Group	Baseline	Treatment	Change[b]	*p*-Value[c]
Total chloesterol, mg/dL	16	Distilled	175.7 ± 6.23	179.7 ± 5.15	+4.0	
	16	2 ppm Monochlor	182.7 ± 8.75	182.2 ± 9.54	−0.5	0.23
	16	15 ppm Monochlor	186.8 ± 9.91	193.8 ± 10.11	+7.0	
HDL cholesterol, mg/dL	16	Distilled	46.4 ± 2.47	48.4 ± 2.71	+2.0	
	16	2 ppm Monochlor	47.6 ± 2.57	47.4 ± 2.36	−0.2	0.08
	16	15 ppm Monochlor	46.8 ± 2.00	47.2 ± 1.99	+0.4	
LDL cholesterol, mg/dL	16	Distilled	113.6 ± 5.81	116.6 ± 5.24	+3.0	
	16	2 ppm Monochlor	119.4 ± 7.78	119.9 ± 8.38	+0.5	0.52
	16	15 ppm Monochlor	124.4 ± 9.79	128.8 ± 10.62	+4.4	
Triglycerides, mg/dL	16	Distilled	81.3 ± 7.55	74.0 ± 6.13	−7.3	
	16	2 ppm Monochlor	78.6 ± 11.94	74.8 ± 11.04	−3.8	0.07
	16	15 ppm Monochlor	79.0 ± 15.67	85.0 ± 17.75	+6.0	
LDL:HDL ratio	16	Distilled	2.57 ± 0.20	2.54 ± 0.19	−0.03	
	16	2 ppm Monochlor	2.58 ± 0.20	2.59 ± 0.21	+0.01	0.38
	16	15 ppm Monochlor	2.79 ± 0.30	2.87 ± 0.33	+0.08	
Apolipoprotein A_1, mg/dL	16	Distilled	126.7 ± 2.97	127.7 ± 2.82	+1.0	
	16	2 ppm Monochlor	127.8 ± 3.76	125.5 ± 3.63	−2.3	0.30
	16	15 ppm Monochlor	124.5 ± 2.74	126.0 ± 2.80	+1.5	
Apolipoprotein A_2, mg/dL	16	Distilled	40.1 ± 2.73	41.0 ± 2.55	+0.9	
	16	2 ppm Monochlor	37.4 ± 1.16	38.5 ± 1.51	+1.1	0.95
	16	15 ppm Monochlor	38.2 ± 2.64	39.1 ± 2.65	+0.9	
Apolipoprotein B, mg/dL	16	Distilled	99.9 ± 7.17	98.2 ± 5.35	−1.7	
	16	2 ppm Monochlor	102.8 ± 7.50	101.2 ± 7.28	−1.6	0.02
	16	15 ppm Monochlor	104.2 ± 7.60	116.4 ± 9.45	+12.2	
T4, μg/dL	16	Distilled	6.89 ± 0.21	6.80 ± 0.23	−0.09	
	16	2 ppm Monochlor	6.90 ± 0.12	6.71 ± 0.18	−0.09	0.28
	15	15 ppm Monochlor	7.04 ± 0.23	7.02 ± 0.22	−0.02	
T3, ng/dL	16	Distilled	127.0 ± 4.99	125.5 ± 4.60	−1.5	
	16	2 ppm Monochlor	123.0 ± 4.37	121.6 ± 3.86	−1.4	0.98
	15	15 ppm Monochlor	120.6 ± 3.95	119.1 ± 3.96	−0.5	
T3 Resin uptake, %	16	Distilled	98.4 ± 3.28	98.3 ± 3.22	−0.1	
	16	2 ppm Monochlor	99.1 ± 1.83	98.8 ± 1.90	−0.3	0.92
	15	15 ppm Monochlor	97.4 ± 2.16	96.8 ± 2.13	−0.6	
Thyroid-stimulating hormone μU/mL	16	Distilled	2.60 ± 0.21	2.61 ± 0.21	+0.01	
	16	2 ppm Monochlor	2.69 ± 0.21	2.60 ± 0.18	−0.09	0.68
	15	15 ppm Monochlor	2.75 ± 0.25	2.75 ± 0.26	+0.00	

[a]Mean ± SEM for each parameter.
[b]Change = treatment (week 8) − baseline (week 4).
[c]The *p*-value shown is the probability that the change values for the three groups are the same (one-way analysis of variance).

lipid or thyroid metabolism except apolipoprotein B. A modest increase in apolipoprotein B concentration was observed in the group that drank water containing 15 ppm monochloramine. The individual apolipoprotein data were examined for each of the subjects in the 15 ppm group to see whether this change in the mean value was due to a large change in a few subjects or more modest changes in many subjects. Eleven of 16 increased while five of 16 decreased. Six subjects increased more than 10%, while only one subject decreased by more than 10%. Thus, the observed change in mean apolipoprotein B levels was not due to a large change in one or a few individuals.

Apolipoprotein B is found in LDL and VLDL (very low-density lipoprotein). In the fasting state, most of the plasma triglycerides are carried by VLDL; thus, triglyceride concentrations are a good surrogate for VLDL concentrations (as long as triglycerides are less than 400 mg/dL). There was a trend toward increased triglyceride concentrations (and presumed increased VLDL) in the 15 ppm group but no change in LDL. This might suggest that the increase in apolipoprotein B was due to an increase in VLDL. However, there was only a borderline correlation between changes in triglycerides and changes in apolipoprotein B in the 15 ppm group (Pearson $r = 0.45$; $p = 0.08$), which depended almost entirely on the results from one subject. If the data for this subject were excluded, no correlation existed. In contrast, even though mean LDL did not increase, there was a correlation (Pearson $r = 0.56$, $p = 0.02$) between individual changes in apolipoprotein B and LDL cholesterol concentrations for the men exposed to 15 ppm monochloramine, which did not depend on the results of any one subject.

The chloramine solutions were well tolerated by the subjects. No new, significant abnormality in any safety test was noted in any subject. Two subjects in the distilled water group, two subjects in the 2 ppm chloramine group, and three subjects in the 15 ppm chloramine group experienced intermittent diarrhea (2–10 episodes) during the study. Two subjects in the 15 ppm group developed a sore throat with exposure to monochloramine, and two experienced intermittent mild headaches. These effects were not noted in the other groups. The dose of monochloramine had to be reduced to 7.5 ppm for a total of 6 days for one of the 15 ppm subjects with a sore throat because he believed the disinfectant was the cause of his symptoms.

Discussion

The short-term (4 weeks) consumption of drinking water containing 2 ppm monochloramine did not affect any parameters of lipid or thyroid metabolism in the healthy men studied. The short-term consumption of drinking water containing 15 ppm monochloramine was associated with an increase in the level of plasma apolipoprotein B, but there were no significant changes in other parameters of lipid and thyroid function.

These results with 2 ppm monochloramine are consistent with the negative results we have found previously with short-term exposure of healthy men and women to drinking water chlorine with a concentration of 20 ppm (*5*). The increase in the level of apolipoprotein B observed in men drinking 15 ppm monochloramine contrasts with our results with drinking water chlorine, where we observed no changes in apolipoprotein B. The other studies of the lipid effects of chlorinated disinfectants cited in the Introduction did not include apolipoprotein measurements (*2,3,6*).

Apolipoprotein B is a protein found only in LDL and VLDL lipoproteins (*15*). There is exactly one apolipoprotein B molecule in each LDL particle. The number of apolipoprotein B proteins associated with each VLDL particle is unknown, though it probably is one also since VLDL particles are converted to LDL particles in the blood as triglycerides are removed from them, and no addition or removal of apolipoprotein B is thought to occur during this process. If the composition of the LDL and VLDL particles remained unchanged, an increase in apolipoprotein B would be associated with an increase in LDL cholesterol concentration, an increase in triglycerides (since almost all of the triglycerides in the fasting state are in VLDL particles), or an increase in both. No change in calculated LDL cholesterol concentration was apparent in the 15 ppm group. There was a trend toward increased triglycerides in this group, though the magnitude of this apparent change was small, the trend did not reach statistical significance, and the correlation was completely dependent on the results from one subject. There was, however, a good correlation between changes in apolipoprotein B and changes in LDL cholesterol. In other words, subjects who experienced an increase in apolipoprotein B levels also tended to experience an increase in LDL cholesterol levels even though the group means for LDL cholesterol did not reflect these changes. One explanation for an observed change in apolipoprotein B without a statistically significant change in LDL cholesterol is that apolipoprotein B levels may be a more sensitive and accurate marker for LDL levels and that the LDL cholesterol concentrations were not sensitive enough to demonstrate a change. Another explanation is that the composition of LDL lipoproteins can vary. If the composition of LDL particles changed such that less cholesterol was present in each particle, then it would be possible to have an increase in the number of particles without an associated equivalent increase in plasma LDL cholesterol concentration.

Because the study protocol involved 11 planned comparisons of parameters among the groups, the finding of an effect on apolipoprotein B levels could represent a chance result rather than a real change. Thus, additional studies to confirm this finding are required.

The principal limitations of this study include *a*) the relatively brief baseline and treatment periods and *b*) consumption by almost all subjects of chlorinated drinking water from local water supplies before entry into the protocol. The duration of the 4-week baseline period may not have been sufficient to achieve adequate washout of the effects of previously ingested chlorine. Alternatively, the 4-week treatment period may have been too brief to see an effect from exposure to monochloramine. The length of the baseline and study periods was chosen based on the clinical observation that most factors that affect blood cholesterol levels, including diet, do so within a time span of 4 weeks (*16*). Also, practical considerations involved with studying normal human subjects limited the maximum possible length of exposure.

In summary, this randomized, controlled trial failed to show any effect of drinking water monochloramine at a concentration of 2 ppm on parameters of lipid or thyroid metabolism in healthy men. Drinking water monochloramine at a concentration of 15 ppm was associated with an increase in apolipoprotein B levels. Given the limitations of this study, these results argue against changes in disinfection practices involving low levels (2 ppm or less) of monochloramine and argue for further studies of the

possible relationship of high-level exposure to monochloramine and apolipoprotein B metabolism.

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